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UNITED STATES.

THE BACILLUS ICTEROIDES AND ITS RELATION TO YELLOW FEVER.

PARIS, FRANCE, *August 20, 1900.*

SIR: I have the honor to submit herewith a paper by Proust and Wurtz, on the subject of yellow fever, read before the International Congress of Hygiene and Demography.

The conclusions reached by the authors are of special importance in confirming the cause of yellow fever.

Respectfully,

M. J. ROSENAU,
Passed Assistant Surgeon, U. S. M. H. S.

The SURGEON-GENERAL,
U. S. Marine-Hospital Service.

YELLOW FEVER.

By PROUST AND WURTZ.

[Translated by M. J. Rosenau, Passed Assistant Surgeon, U. S. M. H. S.]

Of the three great epidemic diseases of the tropics, plague, cholera, and yellow fever, it is the last whose manifestations during the past years have been least widespread.

Plague, since 1894, has spread from Indo-China into India and from Bombay to the four quarters of the globe. Cholera has reappeared in India with formidable intensity.

On the contrary, yellow fever, if we may except the large number of cases which occurred in the Cuban campaigns and which decimated to a dreadful extent the Spanish and American troops, does not seem to

have spread alarmingly as we have observed more particularly in the case of bubonic plague.

On account of the restraint imposed upon the countries where yellow fever is epidemic (Central America and certain portions of the eastern coast of South America as well as the western coast of Africa) it has not made its appearance in Europe for a long time. So rigidly has this restraint been enforced that it has been possible to discontinue without inconvenience the international prophylactic measures taken to prevent the introduction of the disease into France.

Since the International Congress of Hygiene of 1889, the etiology of two of these formidable tropical epidemics has been demonstrated. The bacillus of bubonic plague was discovered by Yersin and Kitasato at Hongkong in 1894, and this discovery has been unanimously confirmed by bacteriologists throughout the world.

On the other hand, in 1897, Sanarelli announced the discovery of the organism pathogenic for yellow fever. Although this discovery has been less widely and less brilliantly confirmed than that of the bacillus of Yersin, it remains without doubt that the menace of the extension and the dramatic reawakening of plague which lay dormant for so long has made yellow fever of secondary importance.

The microbe isolated by Sanarelli, which he considers specific for yellow fever, has been called by him bacillus icteroides. It is found in the blood and in the tissues of individuals sick or dead of yellow fever and not in the gastrointestinal cavity. It is always associated with other microbes.

This fact makes it very difficult to recover it from the cadavers of subjects dead of yellow fever. Its dissemination in the organism is, in fact, very transitory. Sanarelli established this interesting fact experimentally by killing daily animals inoculated with this bacillus. From the second to the seventh day the bacillus icteroides is found only in the spleen; after that time the bacillus invades the whole organism.

The constant presence of microorganisms of secondary infection is a singular complication in the search after the specific bacillus, and it is this special property of this organism as well as of its toxin, that favors secondary infections. This phenomenon is constant, not only in man, but also in the majority of animals inoculated experimentally.

In man, Sanarelli found the bacillus in but half the cases which he examined.

The bacillus icteroides is a rod with rounded ends frequently united in chains two to four long. Its dimensions vary. It is motile and has cilia.

Cultures on gelatin plates give punctiform colonies having the appearance and dimensions of a leucocyte. They are, in fact, round, colorless, without nucleus, and show a very fine, brilliant granulation. The bacillus never liquefies gelatin.

In the center of the colony there appears, about the sixth or seventh day, a characteristic black spherical point.

The colonies may also present atypical forms differing considerably from the ordinary (concentric rings in rosette, nucleus tangled reticula).

The colonies always keep their granular and brilliant appearance, and never take the yellow-brownish color that is observed in cultures of the colon bacillus.

Cultures of the bacillus icteroides which have grown on agar at 37° C., become thicker and whitish, in contrast to the original culture, and take the "seal ring" appearance.


17° 30' N.
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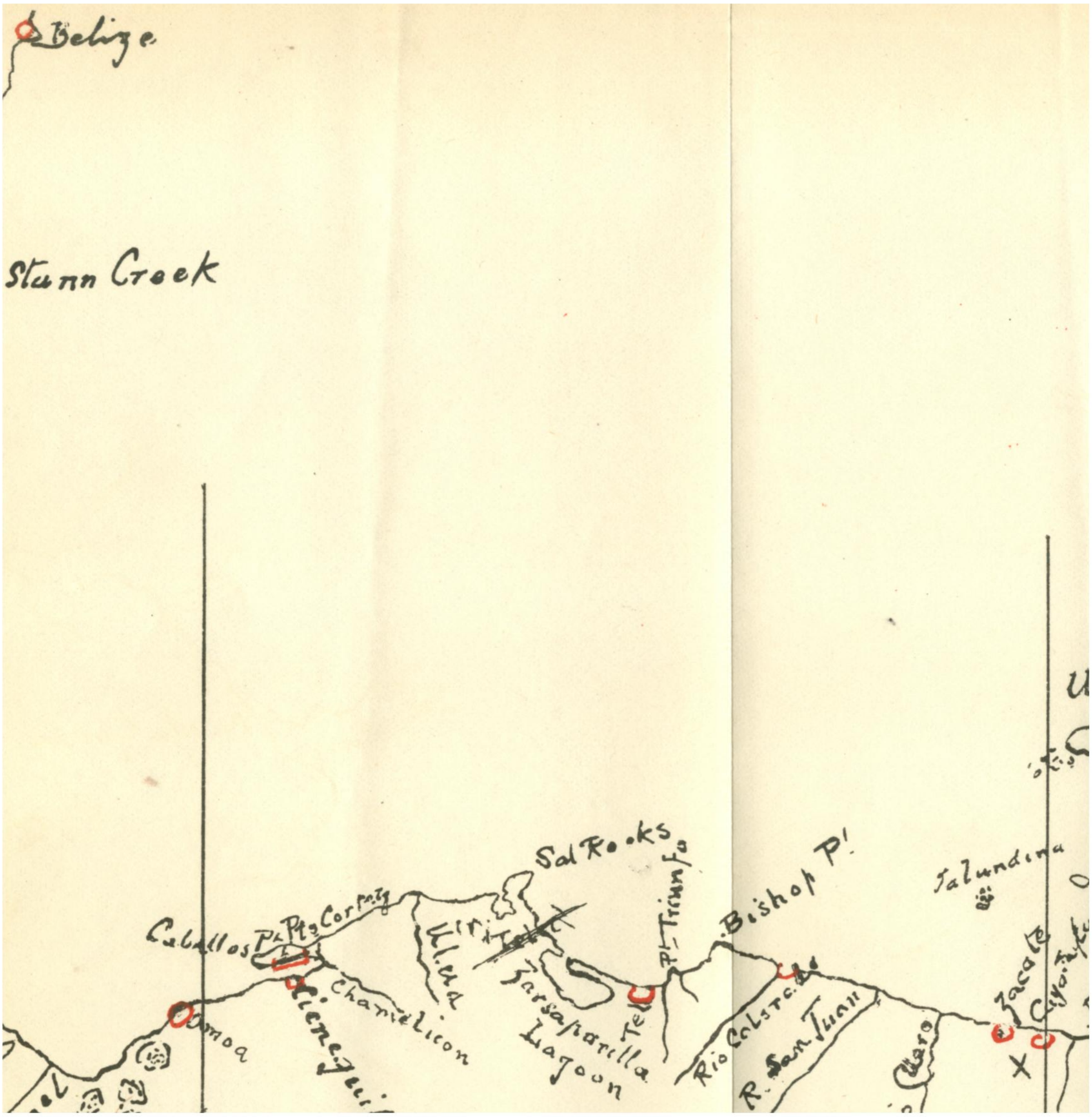
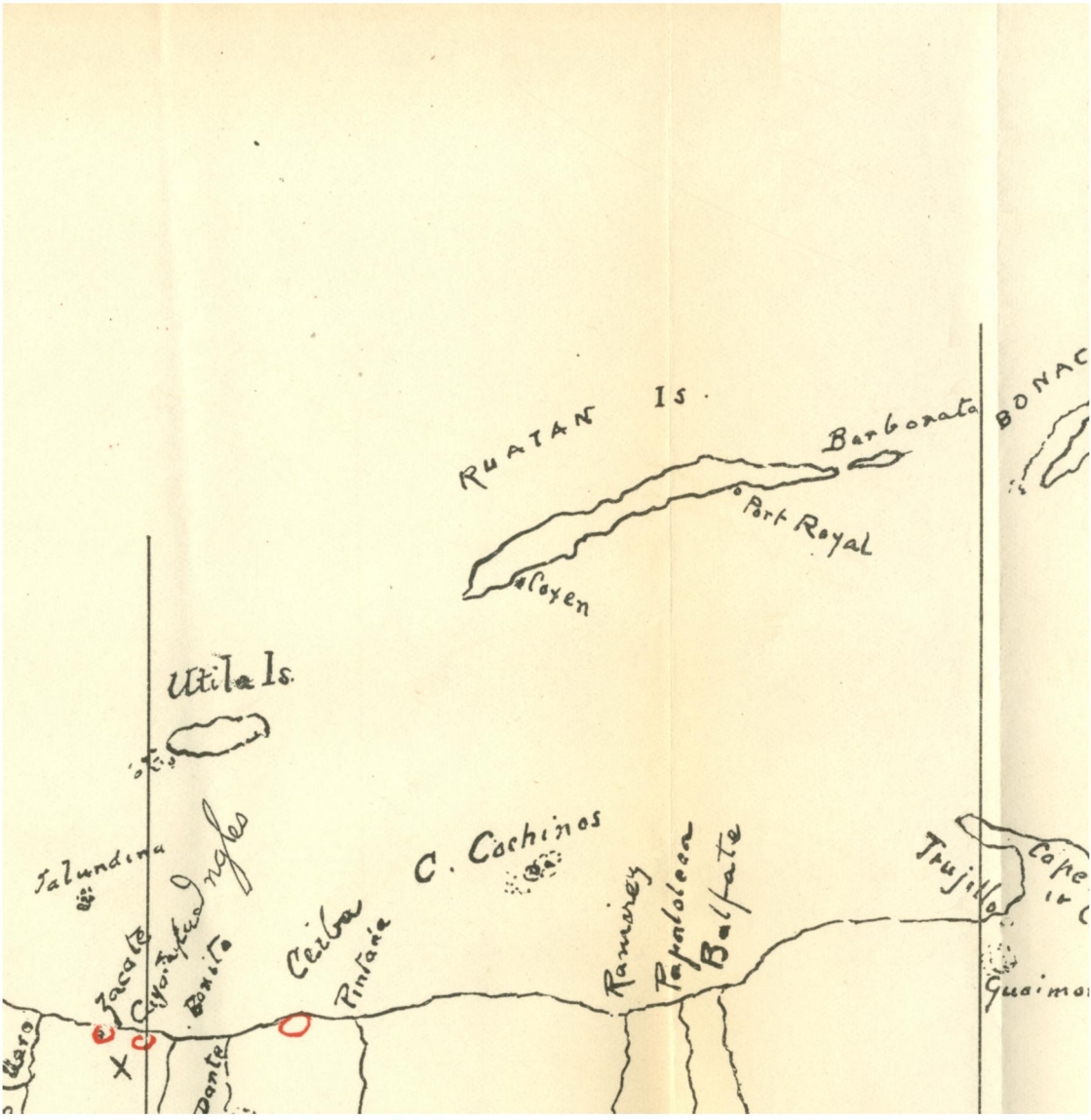
Stann Cree
Monkey River
Punta Gorda
Moho River
Three Points
Livingston
Plc Barrios
San Francisco R.


Belize
Stann Creek
Sal Rocks
Bishop Pt
Caballos
Omoa
Chamelicon
Ulua
Sarsaparilla
Lagoon
Tela
R. San Juan
Zacate


RUATAN Is.
Barbonata
BONAC
Port Royal
Coxen
Utila Is.
Salundina
Zacate
Cayetano Inglés
Bonito
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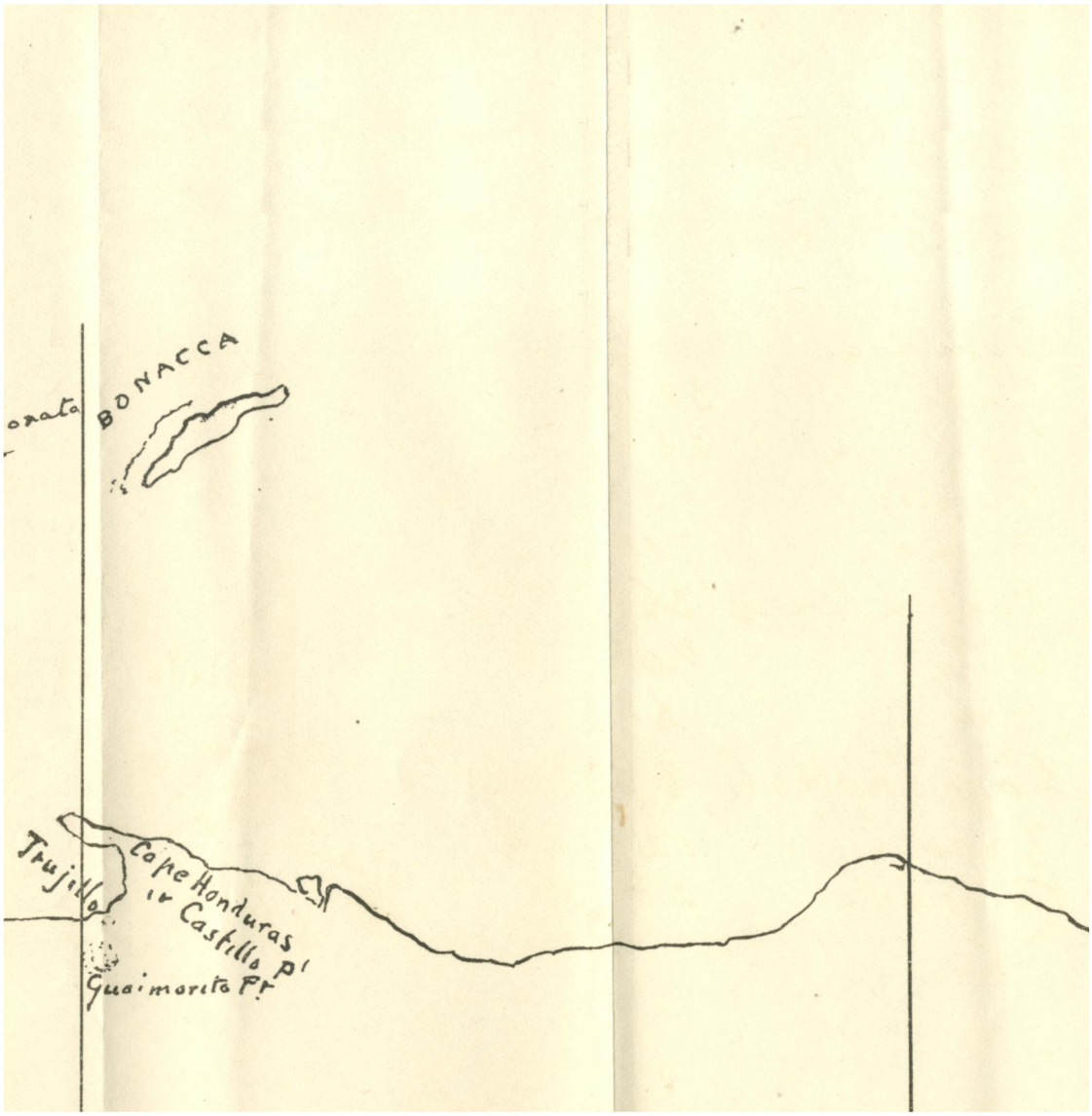
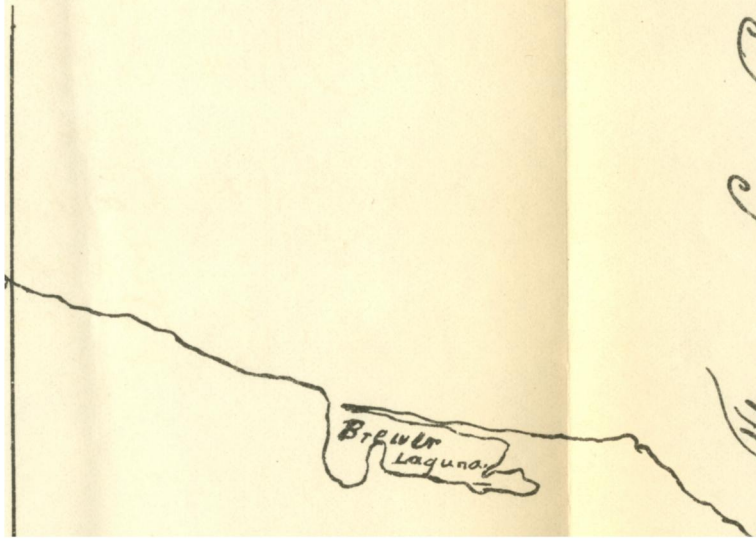
Pinfarie
C. Cochinos
Ramirez
Papalotean
Balfate
Trujillo
Guaimo


BONACCA
Trujillo
Cape Honduras
or Castillo Pt
Guaimorita Pt



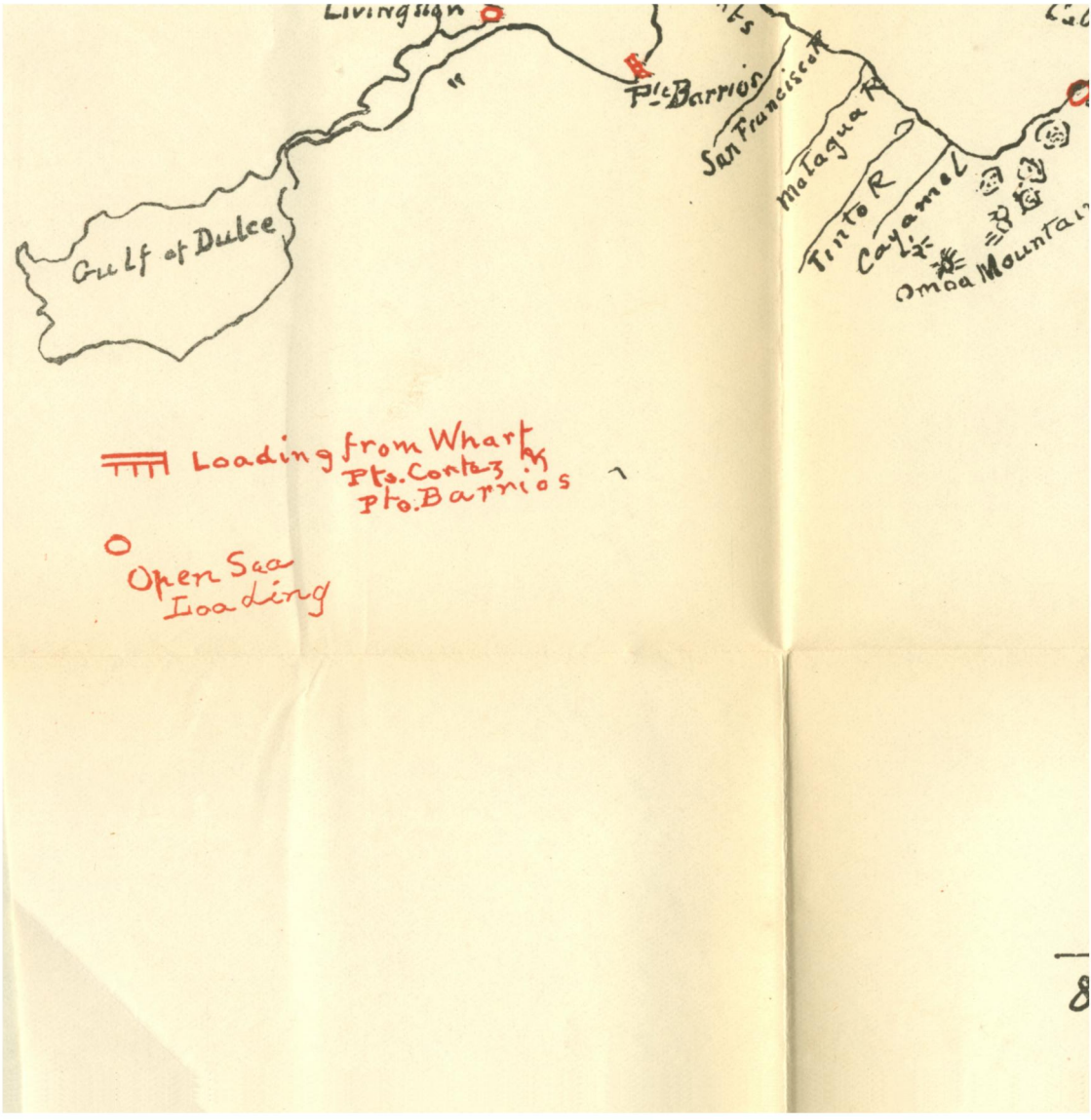
Distances

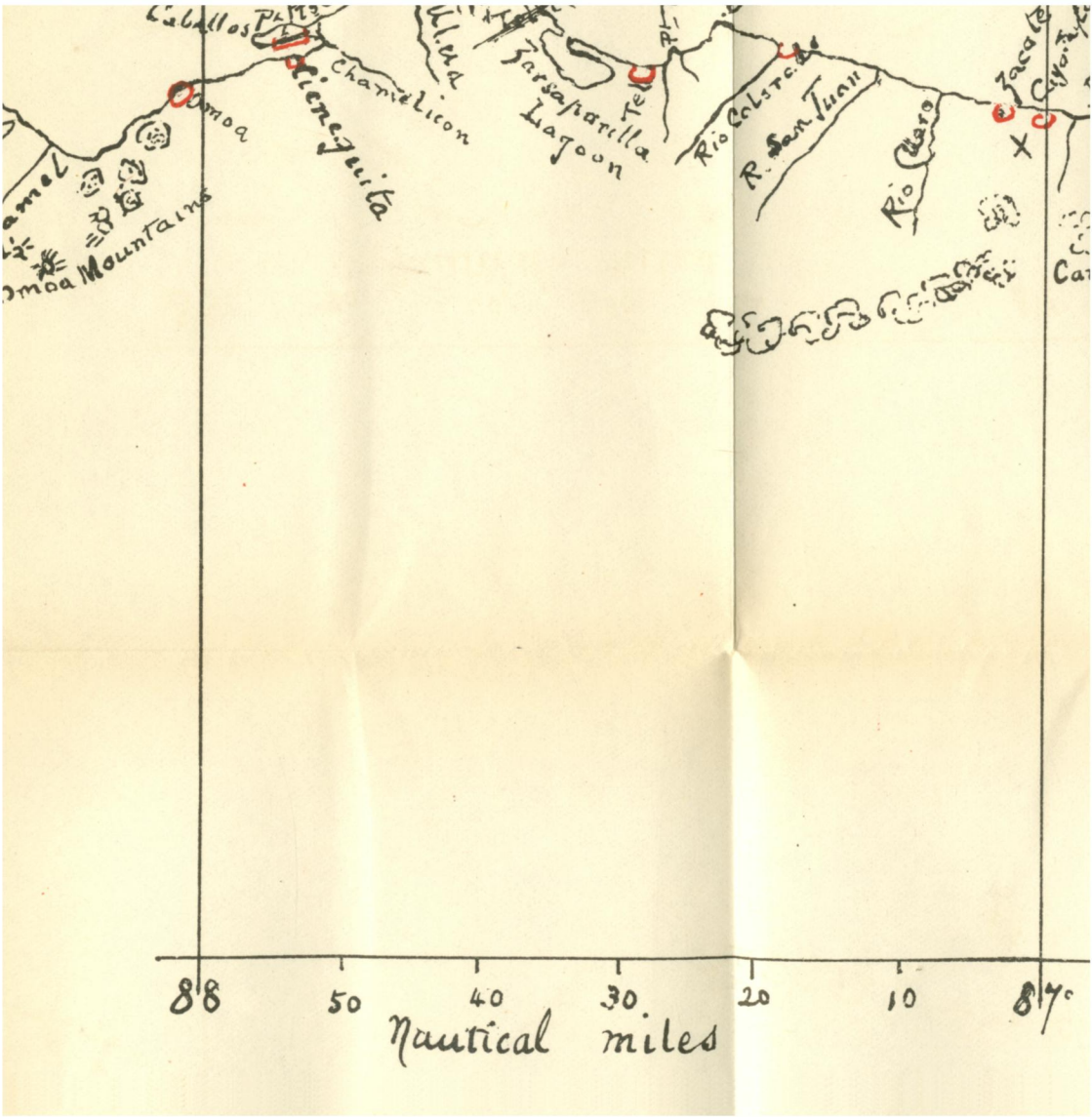
From La Ceiba

to La Punta
" Balfa
" Papalo
" Trujil
. Bona
.. Ruata
* Utila
" Boni
x" Cayo
x" Zaca
x . Colora
x .. Tela
x .. Puerto
x Cieneg

ances from Ceiba Rep. of Hond.

La Rintada	6	miles
Balfata	32	"
Papaloteca	28	"
Trujillo	55	"
Bonaca	71	"
Ruatan (Coxen)	36	"
Utila	20	"
Bonito	6 1/2	"
Cayo Inglés	8 1/2	"
Zacate	12	"
Colorado	28	"
Tela	50	"
Puerto Cortez	69	"
Cienegueta	70	


Livingston
Pto Barrios
San Francisco
Motagua R
Tinto R
Cayamel
Omoa Mountains
Gulf of Dulce
Loading from Wharf
Pts. Cortez
Pto. Barrios
Open Sea
Loading


Caballos
Omoa
Omoa Mountains
Chamelicon
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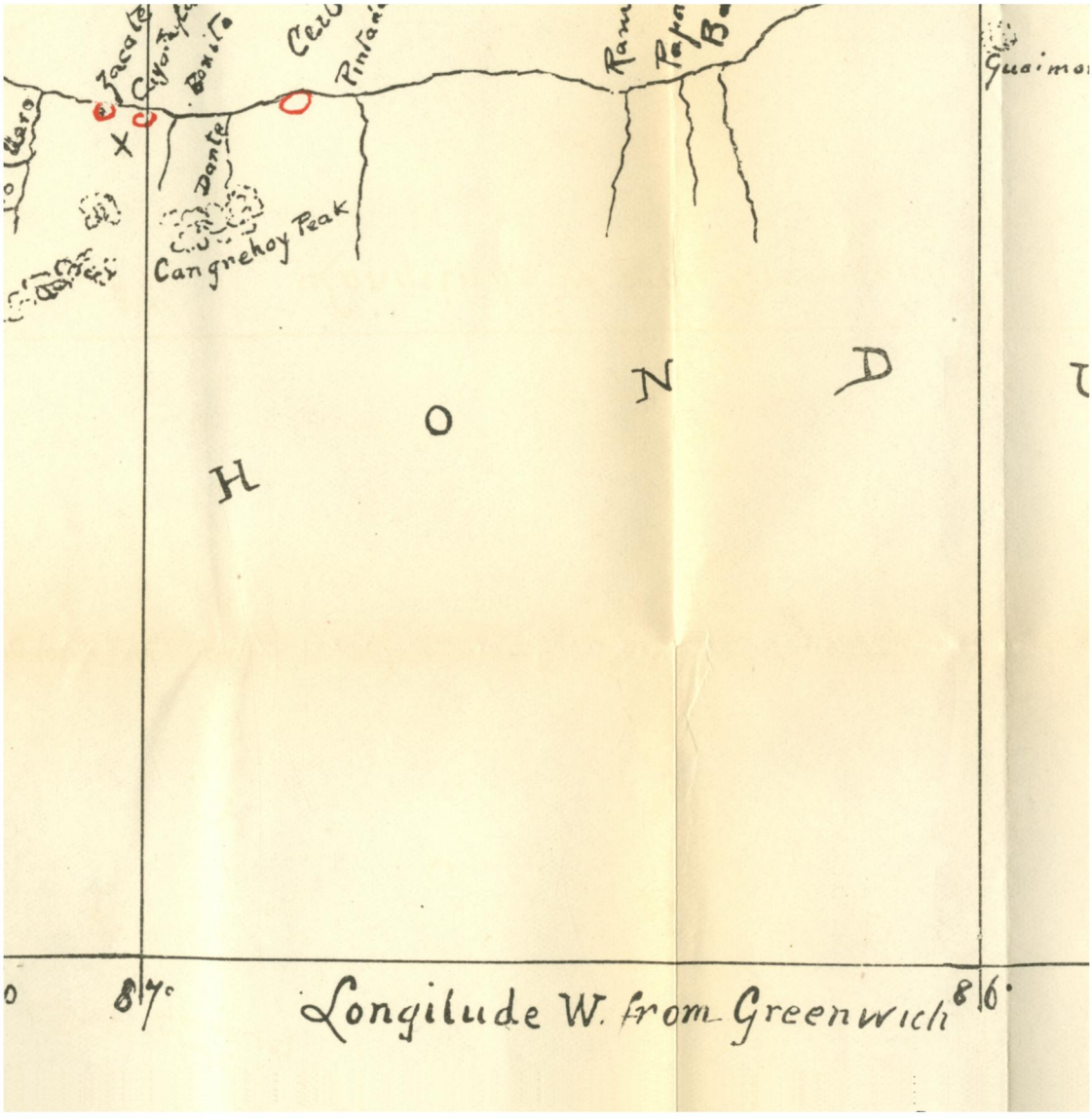
Nautical miles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Cangrehoy Peak
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Longitude W. from Greenwich
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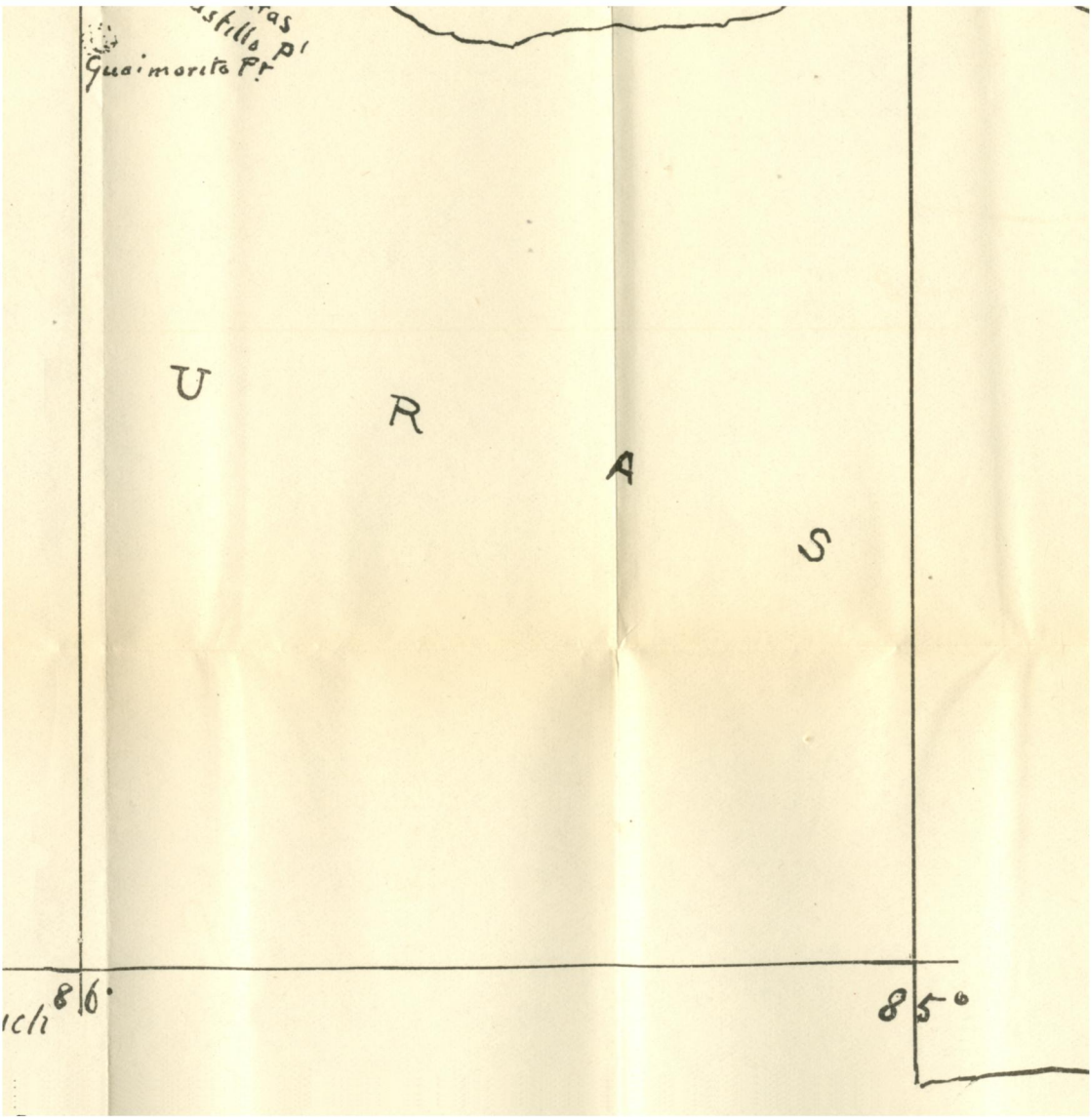
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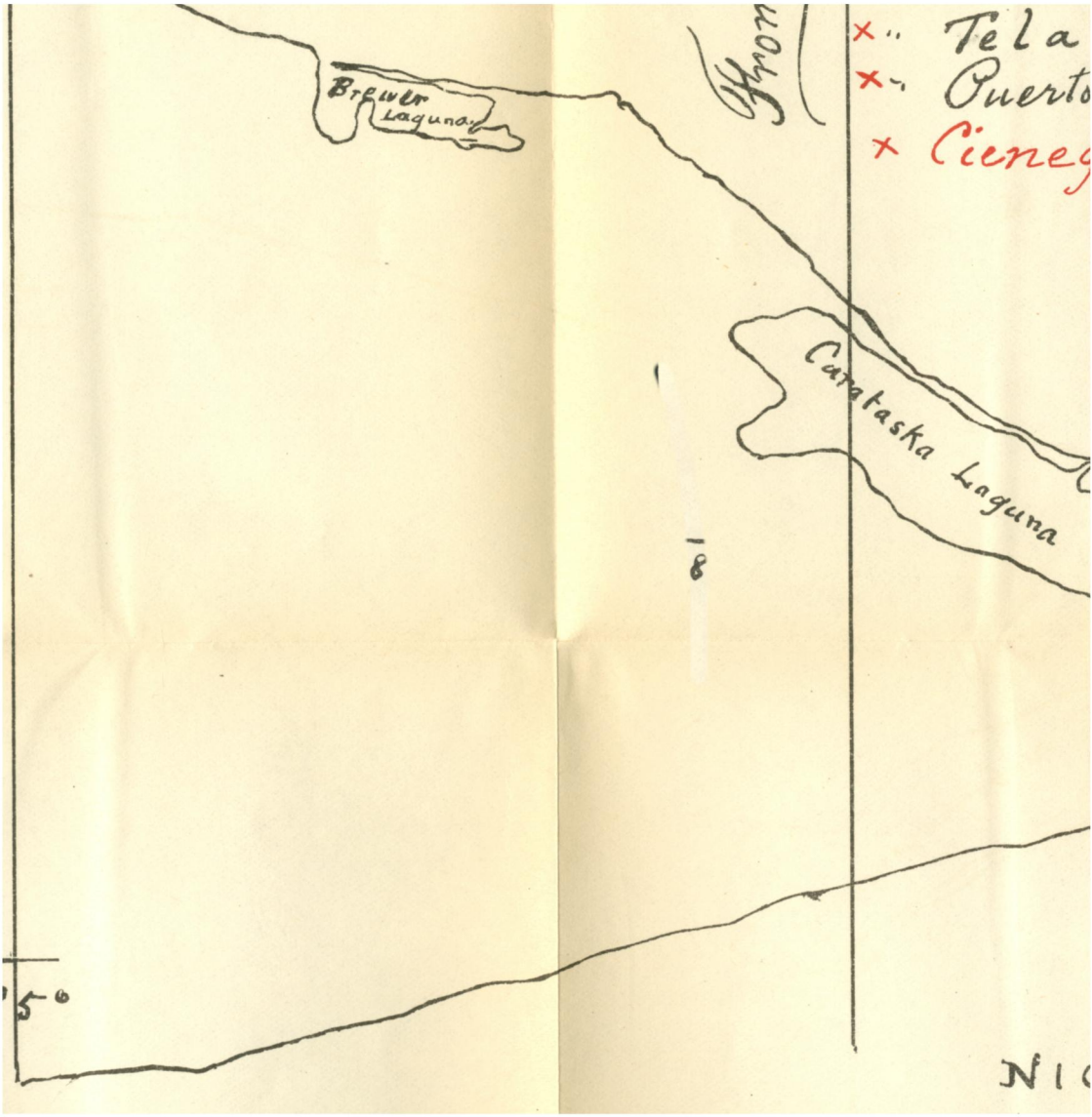
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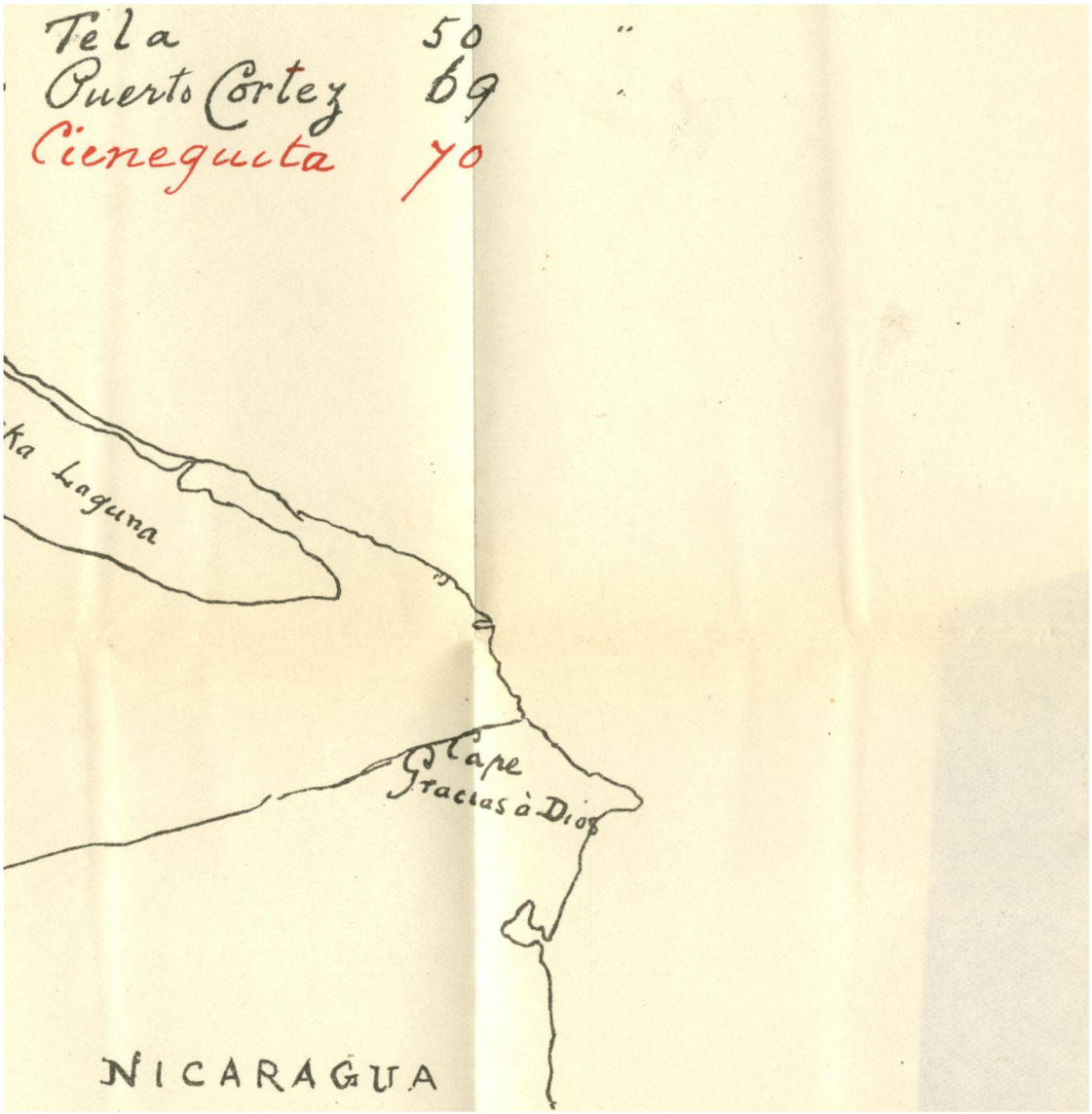
Tela 50 "
Puerto Cortez 69
Cieneguita 70
ka Laguna
Cape
Gracias à Dios
NICARAGUA

This appearance of the cultures on agar is considered by Sanarelli the most typical characteristic of the cultures of bacillus icteroides.

It grows best in lactose bouillon with the addition of 2 per cent carbonate of lime.

The bacillus icteroides is a facultative anærobe. It stains well with all of the basic anilin dyes and does *not* stain by Grams's method.

Among the biological properties of bacillus icteroides there are some that have a particular interest.

Spontaneous desiccation at ordinary temperatures leaves the bacillus icteroides with considerable vitality (seven months). *It is known that the bacillus survives a much longer time in nature than is indicated by the results obtained in the laboratory, which explains the reappearance of the disease after several years.*

The resistance to dry heat is considerable; it takes an hour and ten minutes to kill it at a temperature of 100° C.; at 120° to 125° C. the bacillus icteroides dies quickly. On the other hand, its resistance to the sun is inconstant but weak—it dies in summer after seven hours at a temperature of 28° C.

The physical agent which acts the most surely and rapidly is moist heat. In water at 60° C. the bacillus icteroides dies in a few minutes, and immediately at 65° C. Boiling water, therefore, is the best disinfectant for yellow fever.

Sanarelli has further demonstrated that in media the presence of moulds favors the development of the bacillus icteroides considerably. On plates inoculated but not showing a growth the bacillus may be brought to life by sowing any kind of mold on the plate.

The development of molds, being favored, as is known, by heat, moisture, and lack of ventilation, would be indirectly favorable to the development and multiplication of the bacillus icteroides.

Humidity should be, then, one of the most active causes in the development of yellow fever.

The bacillus of yellow fever lives in sea water for a very long time. This confirms what has been known for a long time of the development of yellow fever in seaports.

The bacillus icteroides is pathogenic for most of the domestic animals. Birds are completely refractory. In mice, guinea pigs, rabbits, and especially in dogs and in monkeys it causes a cyclic disease analogous to that observed in man.

The bacillus, therefore, possesses 3 principal pathogenic properties, which together give it characteristics which could almost be considered specific. These properties are steatogenic, congestive, hemorrhagic, and emetic.

The filtered culture of the bacillus icteroides contains an extremely active toxin, and when injected, into the dog in particular, produces the same symptoms and the same lesions as the bacillus.

Finally, Sanarelli injected 5 individuals with a bouillon culture fifteen to twenty days old, filtered and sterilized with several drops of formic-aldehyd. The injection of filtered culture in relatively small doses produced typical yellow fever, accompanied by all its symptoms and anatomical conditions.

It is to be noted, however, that of the 5 individuals injected, 3 subcutaneously into the cellular tissue, 2 into veins, but 1 showed the clinical aspect of yellow fever.

The bacillus icteroides was discovered in 1897; in three years a certain number of researches have been made confirmatory of that of Sanarelli.

The first point to verify was whether bacillus icteroides is found in the organs of those sick or dead of yellow fever. This was found to be the fact in the work of Pothier (52 autopsies), Hamilton Jones, Archinard, Geddings, Wasdin, Mendoza, Guberrier, and Pieto Ramos. The bacillus icteroides was isolated by these different authors in a variable proportion, sometimes in almost all the cases examined; 32 in 39 (Archinard); 79.93 per cent (Geddings); 70 per cent (Horlbeck), and by the commission of the United States Marine-Hospital Service, 100 per cent during one year in Cuba.

In France, M. Gauthier isolated the organism from a patient sick of yellow fever. The patient arrived at Marseilles on the packet *Provence*, on which a little epidemic of yellow fever existed. Therefore the presence of the bacillus icteroides has been confirmed a very large number of times, both during life and after death.

A relatively limited number of bacteriologists have studied yellow fever in the epidemic foci during the past three years.

But the cultures of the bacilli isolated, both by Sanarelli and by the authors mentioned, have been studied with confirmatory results as far as the biological properties of this bacillus are concerned. Lacarda, Foa, Belfanti and Renoud, Rovere and more recently Bruschettini have studied the morphology, the pathogenesis, the toxins of the bacillus icteroides. All have confirmed the facts announced by Sanarelli, and they have completed the work in certain details—inoculations of birds, etc.

The conditions necessary to consider a microbe specific for a certain disease are the following: The microbe must be found in every case of the disease, and in these cases only. The inoculation of the microbe into animals must reproduce the lesions and the symptoms of the disease.

Now these conditions are filled in the case of the bacillus icteroides. That it has not been isolated in every case of yellow fever examined bacteriologically is due to the difficulties of the work caused largely by the secondary infections.

The experimental disease is almost identical with that in man. The injection of the toxin in man reproduces the symptoms of yellow fever.

Further, the serum of individuals attacked by yellow fever agglutinates the bacillus icteroides (Archinard and Woodson, Sanarelli, Foa, Mendoza). This specific reaction seems to us to be the decisive proof that the bacillus icteroides discovered by Sanarelli is the cause of yellow fever.

The mode of its entrance into the organism does not seem to be definitely decided. Laboratory experiments have demonstrated the possibility of infection by inhalation.

The infection by water as well as the infection by the air have not been demonstrated in man.

The soil, especially newly worked earth in the neighborhood of cadavers dead of yellow fever, seems to have played an important rôle in the spread of the infection in certain African epidemics (Soudan, 1897, Auvray and Boury).

This infection actually took place by direct contact (hands) or by inhalation.

The theory of Finlay, that the mosquito plays an important rôle as a carrier of yellow fever, has not furnished any of the proofs that have accumulated for malaria. Finlay has recently expressed the opinion that the mosquito has the power of transmitting the contagion by its

eggs. Before accepting this view it will be necessary to confirm in all instances the presence of the infectious agent.

Although we now believe that we know the specific cause of yellow fever, it must be admitted that from the point of view of prophylaxis less progress has been made than from the etiological standpoint. There is nothing to change in the prescribed measures for preventing yellow fever. Disinfection is equally efficacious against an unknown infectious agent as against a well-described and thoroughly studied microbe.

"Humidity, heat, darkness and lack of air seem to be the most favorable factors for the bacillus icteroides." Epidemiologists knew this long ago. Sanarelli has given a new explanation of the resistance of the bacillus icteroides and its mysterious longevity on board of vessels. That is to say that ordinary moulds of the air favor the development of the bacillus icteroides.

The sanitary measures actually employed are therefore the same as formerly, as well as the necessity for the improvement of the hygienic conditions.

As far as individual prophylaxis is concerned, Sanarelli shows, in his last communications, that this important problem has not yet been solved. He hopes to arrive at a solution by means of serum therapy.

The difficulty is to make animals tolerate heavy doses of the icteroides and to obtain a serum having both preventive and curative power. "The serum acts against the microbes but can not destroy their toxins once they are formed." The serum, then, acts only as a preventive and can have curative power only when employed very early. However this may be, of the first group of 8 cases (Hospital de San Sebastien at Rio Janeiro) 3 were treated at the commencement of the disease, 1 on the second day, 2 on the third day; of these, 3 recovered. Of 5 treated on the fourth day by 80 c. c. of serum there were 4 recoveries.

Of a second group of 22 cases (Ville de San Carlos), where the average mortality is 80 to 90 per cent instead of 50 per cent, as it is on the coast, 2 children treated at the commencement of the disease, on the second and third day, recovered; 4 out of 6 adults recovered under similar conditions. The serum injected intravenously resulted in 10 cures out of 14 treated.

From the point of view of the prophylactic value of the serum, we recall the experience in San Carlos prison where 4 cases appeared within several days. All the prisoners and 2 soldiers were injected with antiamaryllic serum. There was not another case.

Conclusions.

I. The bacillus icteroides, discovered by Sanarelli, seems to us to be the specific agent of yellow fever.

That microorganism injected into certain animals, especially dogs, reproduces symptoms and lesions strikingly analogous to those observed in man.

The toxin of this bacillus produces in animals the same effects as the microbe. The injection of this toxin into 5 individuals reproduced in man typical yellow fever, accompanied by its symptoms and anatomical lesions.

The serum of individuals attacked with yellow fever agglutinates cultures of the bacillus icteroides.

II. The bacillus has a prolonged vitality both in air and water (fresh

and sea). It is certain that it is the same in the soil. Moulds favor its development. These facts confirm conditions that have been known a long time. They explain the reawakening of yellow fever a long time after the extinction of an epidemic, and the longevity of the disease aboard vessels in bad hygienic conditions.

No new prophylactic measures have come out of this knowledge of the etiology of the disease. As formerly, the prevention of yellow fever consists in applying the measures of isolation and of disinfection, and of improving the hygienic conditions.

Quarantine measures against the introduction of plague from Glasgow, Scotland.

Referring to statement of plague in Glasgow on page 2186, PUBLIC HEALTH REPORTS, No. 35, P. A. Surg. A. R. Thomas was detailed by the President for duty in the office of the United States consul at Glasgow, to enforce the Treasury regulations, and arrived in that city August 30, 1900. Acting Asst. Surg. J. S. Hough was ordered on September 1, 1900, from London to Glasgow to assist Dr. Thomas, and Asst. Surg. John F. Anderson was ordered, on September 1, 1900, from Vienna, Austria, to London, and detailed by the President in the office of the consul-general at the latter place to assume Dr. Thomas's duties in his absence. On September 6, 1900, the following message was sent to Dr. Anderson in London: "Communicate with Thomas. Proceed Liverpool, duty on same lines as Thomas. Precautions only against Glasgow. Nominate assistant for London if necessary. Record on bill of health Glasgow passengers."

Dr. Thomas has been requested to wire, on the date of departure, the name and port of destination of each vessel leaving for the United States, which he is now doing.

The *Californian* and *Anchoria* sailed, on August 30, for New York; the *Siberian* for Philadelphia, and the *Orthia* for Baltimore on the same date.

At the request of the secretary of the Canadian department of agriculture, Dr. Thomas has been directed to inspect the Allan and Donaldson lines of steamers sailing from Glasgow for Canada, until the arrival of an officer detailed by the Canadian authorities.

Dr. Thomas reports that plague has probably been present in Glasgow since August 3. On September 1 he cabled that 1 additional case of plague had been discovered that day in the case of a person previously held for observation, and that the situation was hopeful. On September 3 he again cabled that no new cases had occurred that day, but that there had been 1 suspicious death at Govan, a small place in the vicinity of Glasgow.

The following order has been cabled to Dr. Thomas:

Make 4 freight classes, (1) free list; (2) inspection and certificate; (3) disinfection and certificate; (4) debarred. Have certificates presented with manifest when you inspect vessel, thus showing exact state of cargo. Disinfect baggage of Glasgow steerage, but all transit and